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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,027	03/26/2002	William E. Jack	NEB-166-PUS	9409

28986 7590 06/01/2007

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
06/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/089,027	JACK ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,13-22 and 27-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,14-17,19-22 and 27-31* is/are rejected.

7)☒ Claim(s) *13 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment of claims 2, 3, 21 and 22, in the paper of 2/27/2007, is acknowledged. Claims 2-4, 13-22 and 27-31 remain pending and at issue for examination.

Applicants' arguments filed on 2/7/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 13, 18 objected to because of the following informalities:

Claims 13 and 18 are dependent on rejected claims 2 and 3. Applicant's comments regarding this objection are noted.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4, 14-17,19-22 and 27-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action as it applied to previous claims 2-4, 14-17,19-22 and 27-31. In response to this rejection applicants have amended claims 2, 3, 21 and 22 and traverse the rejection as it applies to the newly amended claims.

Applicants noting of the Examiners previous assertion that applicants claim a genus of methods drawn to the use of any "archaeon Family B DNA polymerase" and the Examiners interpretation of this phrase to broadly encompass variants and mutants of naturally occurring archaeon Family B DNA polymerases is acknowledged, as well is the fact that applicants have not in any way denied the interpreted breadth of the claimed genus of methods.

Applicants further note as an initial matter that applicants present claims 2 and 3 encompass only those archaeon Family B DNA polymerases that both (i) are encoded by a nucleic acid that either hybridizes under stringent conditions (claim 2) or exhibits a defined amino acid sequence identity (claim 3) to wild type Vent DNA polymerase; and (ii) have the ability to incorporate acyclonucleotides. Applicants continue to submit that such DNA polymerases are well described in the application; and that thus present claims 2 and 3 meet the Written Description requirement.

In arguing applicants point, applicants state that the Written Description requirement ensures that patent applicants claim subject matter that was "within the possession of the inventors" but that *ipsis verbis* disclosure is not necessary to satisfy

the written description requirement of section 112. Instead the disclosure need only reasonably convey to persons skilled in the art that the inventor had possession of the subject matter in question". Applicants submit that certain court decisions have clarified what is required to satisfy the written description requirement for enzymatic proteins and their use. Applicants further submit that the Patent Offices own Written Description Guidelines provide illustrative examples of claim language for proteins that satisfy the Written Description requirement.

Applicants further reference Invitrogen Corp. v. Clonetech Labs. Inc. 77 USPQ2d 1161 (Fed. Cir. 2005) as a case that closely illustrates applicants position. In applicant's summary of this case, applicants submit that this case was directed to similar claims drawn to a reverse transcriptase ("RT") enzyme modified such that it lacks RNase H activity and that specification provided only one representative species. The court nonetheless found the claims adequately described as the court emphasized that at the time of the invention, the sequences of RT genes were known and members of the RT gene family shared significant homologies from one species of RT to another. The court also emphasized that "the specification also discloses test data that the enzyme produced by the listed sequence has the claimed features - DNA polymerase activity without RNase H activity and the specification provides a single example of a member species with the relevant enzymatic activity. Applicants submit that the instant situation more than satisfies these requirements as the Examiner does not dispute that members of the family have homology. Applicants submit that the instant specification specifically exemplifies a number of species of archaeon Family B polymerases that

exhibit significant identity and similarity to each other at the amino acid level, and are demonstrably different at the amino acid level than non-archaeon Family B polymerases.

Applicants submit that the second requirement of Invitrogen is also satisfied, that the present specification includes not one but at least seven examples of archaeon Family B polymerases that exhibit the claimed acyclonucleotide incorporation properties. Applicants thus submit that the specification thus amply illustrates examples of proteins having the claimed structural features (sequence and/or hybridization) and also have the claimed activity, more than satisfying the second Invitrogen requirement.

Applicant's arguments regarding the Invitrogen case are acknowledged, however, applicants are reminded that this case is based upon a different specification, different art, and different claimed subject matter and the merits of the instant specification must be based upon the current application.

It remains that applicants claimed subject matter is not adequately described based upon the isolated consideration of the common structure shared between the archaeon Family B polymerases. While applicants comments regarding the homogeneity shared between this group of polymerases continues to be acknowledged, such is acknowledged in light of the degree of the vast majority of DNA polymerases, many of which have a high degree of homogeneity and not all of which share the ability to incorporate acyclonucleotides into a DNA fragment. Thus applicants reasoning that the degree of homogeneity between these polymerases would or should afford certain polymerase properties continues to not be persuasive.

With respect to applicants second point related to the instant applications inclusion of at least seven examples of archaeon Family B polymerases that exhibit the claimed acyclonucleotide incorporation properties, it remains that applicants have not described the structure to function relationship for the "incorporation of acyclonucleotides into a DNA fragment". It is this structure to function relationship that would help applicants in the description and enablement of the claimed genus. Applicants pointing out of the structure to function relationship of the archaeon Family B DNA polymerases with respect to general polymerase function continues to be acknowledged, however, not considered sufficient to describe those polymerases that have the necessary function of incorporating acyclonucleotides into a DNA fragment.

Applicants further submit that the Patent Office Written Description guidelines confirms the patentability of the present claims, particularly relevant to Examples 9 and 14. Applicants submit that Example 9 recites hybridization conditions, wherein said nucleic acid encodes a protein [having a particular function]..." when the specification recited only a single nucleotide sequence encoding a protein with the recited function. Applicants submit that, Example 9 states that: "...a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of the DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention." Applicants submit that present

claim 2 has precisely the same type language as that of Example 9 of the Written Description guidelines. Furthermore, present claim 2 is supported by a specification containing not one, but at least six different specific examples of proteins encoded by sequences that hybridize under the recited conditions to the recited example sequence, which proteins also have the recited sequence. Applicants submit that present claim 2 therefore more than satisfies the Written Description requirements set forth in the Patent Office's own guidelines.

Applicants further submit that Example 14 of the Written Description guidelines presents claims that recite proteins based on their function and degree of homology. In that Example, a claim reciting "A protein having SEQ ID NO: 3 and variants thereof that are a least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A ~ B" and such is said to satisfy the written description requirement when the specification recites only a single polypeptide sequence encoding a protein with the recited function.

Applicants submit that present claim 3 has precisely the same language as recommended in Example 14 of the Written Description guidelines. Applicants submit that the degree of identity recited in claim 3 is lower than that in Example 14, however, claim 3 is supported by a specification containing not one, but at least seven different specific examples of proteins having the recited degree of identity and the recited activity. Applicants further submit that the recited relationship between degree of identity and activity is further supported by a sworn Declaration.

With respect to applicants assertion that applicants recited claims are analogous to the claims of examples 9 and 14 of the Patent Offices Written Description Guidelines,

applicants are reminded that these are in fact just that, guidelines, to be used to help one determine whether the claims in question meet the description requirements. In using these guidelines one must look at all aspects of the claimed invention, not only those aspects raised by applicants, i.e. whether structural and functional limitations exist for the claimed genus, but also specifics of the recited structural and functional limitations and the relationship and interaction between the recited structure and the recited function and how this relates to the claimed genus.

Applicants claim 2 recites that the genus of structural limitations is such that the claimed method recites the use of any polymerase which is encoded by a fragment that hybridizes in a Southern blot to an isolated DNA fragment selected from any of a number of nucleotide fragments of a much larger DNA molecule. As such applicants have not adequately described the claimed genus of methods of incorporation of acyclonucleotides into DNA comprising the use of any DNA polymerase which hybridizes to one of the recited fragments. Applicants recited structure and function and more so, the structure to function correlation, is insufficient to adequately describe the claimed genus of methods.

Applicants claim 3 recites that the genus of structural limitations is such that the claimed method recites the use of any polymerase which has a mere 30% primary sequence identity to Vent DNA polymerase. As such applicants have not adequately described the claimed genus of methods of incorporation of acyclonucleotides into DNA comprising the use of any DNA polymerase which has a mere 30% primary sequence identity to Vent DNA polymerase. Applicants recited structure and function and more so

the structure to function correlation is insufficient to adequately describe the claimed genus of methods.

Further still with respect to the recited functional limitations of the required polymerases, it remains that applicants have not adequately described the structure to function correlation claimed with respect to those DNA polymerases that are capable of incorporating acyclonucleotides into a DNA fragment, relative to those that are merely capable of incorporating normal nucleotides into a DNA.

Applicants further submit that the Examiner's earlier and above assertion that "applicants reasoning that the degree of homogeneity between these polymerases would or should afford certain polymerase properties is not persuasive" apparently because some DNA polymerases may have a high degree of homogeneity even though not all share the same activity" flawed for several reasons. First, the present claims are limited only to polymerases that do in fact share both sequence homology and activity and secondly, that the Examiner is not entitled to ignore the sworn Declaration of an expert in the field definitively stating that there is a relationship between structural homogeneity and functional activity.

Applicants points continue to be recognized, but not found persuasive because just because applicants are limiting the claimed methods to methods of use of DNA polymerases which have a specific function, does not relieve applicants of the need to describe the claimed genus. This is perhaps even more critical in light of the specific function recited and its relevance or association with the larger structural genus of DNA polymerases which do not have such a function.

Thus for the reason previously made of record and repeated herein applicants arguments continue to be found nonpersuasive.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 2-4, 14-17,19-22 and 27-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method for site-specific incorporation of acyclonucleotides into DNA comprising reacting a archaeon Family B DNA Polymerase, a primed DNA template and a nucleotide solution containing the referred to nucleotide to produce fragments of DNA with the referred to nucleotide covalently attached to the 3'-terminal residue, wherein said archaeon Family B DNA polymerase is Vent, Deep Vent, *Pfu* and 9oNTM or the specifically disclosed variants referred to in claim 18, does not reasonably provide enablement for any method for site-specific incorporation of acyclonucleotides into DNA comprising reacting any archaeon Family B DNA Polymerase having the structural and functional limitation recited in claims 2 or 3, a primed DNA template and nucleotide solution containing the referred to nucleotide to produce fragments of DNA with the referred to nucleotide covalently attached to the 3'-terminal residue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action as it applied to previous claims 2-4, 14-17,19-22 and 27-31. In response to this rejection applicants have amended claims 2, 3, 21 and 22 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection by reiterating the arguments presented above relating to the written description requirement in their entirety as they relate to the enablement determination.

In addressing the rejection based upon a lack of scope of enablement, applicants address the Wands factors separately.

The factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Applicants submit with respect to factors (8) the breadth of the claim(s) and (4) the nature of the invention, applicants submit that the general nature of the claimed invention., i.e. reacting a polymerase with a primed template and nucleotides to generate an extension product, is well within the ordinary skill in the art and that the presently pending claims or rather those polymerases necessary to practice the claims

are also within the ordinary skill in the art or at least given the guidance provided by the instant specification.

Applicants are reminded that while the nature of the invention, the synthesis of a DNA is well within the ordinary skill in the art, the incorporation of acyclonucleotides into a DNA or rather those polymerases which are capable of such incorporation is not as equally within the ordinary artisans skill. It continues to be realized that the pending claims are not directed to the use of any polymerase, but rather to a subgenus of polymerases that have a specific function for which insufficient guidance is provided and the breadth of encompassed polymerases encompassed by the claimed methods continues to be excessive.

Applicants submit with respect to factors (5) the state of the prior art, and (7) the predictability or unpredictability of the art, numerous DNA polymerases and their primary amino acid sequences are known in the prior art and the submitted declaration evidences the high degree of primary amino acid and three dimensional structural conservation between archaeon Family B DNA polymerases as well as a physical explanation for the preferential incorporation of acyclonucleotides by members of the genus. Applicants thus submit that the state of the prior art and the level of predictability in the art are sufficient to enable one of ordinary skill in the art to practice the claimed invention.

In response to these assertions, the examiner acknowledges the state of the art, but with respect to predictability of the art, it continues to be questioned as to the basis of those claimed archaeon DNA polymerases that are able to incorporate

acyclonucleotides into a DNA relative to the broadly claimed structural genus(es) in spite of applicants above assertions that the instant claims are analogous to those of examples 9 and 14 in the PTO's Written Description guidelines. This is especially in light of the fact that any structure and function taught by applicants specification does not account for this specialized polymerase function.

The level of skill of one of ordinary skill in the art is recognized to be high, possibly at the Ph.D level.

Finally with respect to factors (1 and 2) the amount of direction or guidance presented, the presence or absence of working examples and (3) the quantity of experimentation necessary to make or use the invention based upon the content of the disclosure applicants continue to submit that applicants specification describes a family of archaeon Family B DNA polymerases, as well as a structure-function relationship between primary amino acid sequence of the archaeon Family B DNA polymerases and their capacity to incorporate acyclonucleotides into a DNA fragment. Applicants continue to assert that the quantity of experimentation needed to make and use the clamed invention is neither excessive nor outside the skill set of one skilled in the art.

Applicants continued arguments and points are completely acknowledged, as are applicants presented declaration and each of these have been considered in full, however taken together these are insufficient to me the rejection based upon a lack of enablement of the scope of the invention. It continues that applicants claimed genus of methods of use of the recited DNA polymerases is excessively broad given to enable the scope of the invention. It continues to be acknowledged that while applicants have

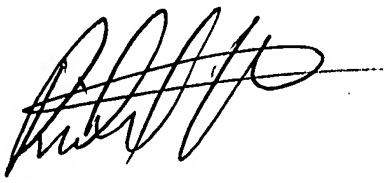
described some structure and function of the family of archaeon Family B DNA polymerase, it remains that they have not enabled one of ordinary skill in the art to make and use those having the necessary acyclonucleotide incorporation properties.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the claimed methods of use of those archaeon Family B DNA polymerase with the specified acyclonucleotide incorporation characteristic. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those methods and polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
5/24/2007